

REMARKS

Status of the Claims

Claims 1-7 and 9-13 were pending and presented for examination in this application. Claims 1-7 and 9-13 are cancelled herein. Claims 14-18 are newly presented. Following entry of the amendment, claims 14-18 will be pending and at issue.

Support for the Amendments to the Claims

Support for new claim 14 can be found throughout the specification as filed, for example, in paragraphs [0017] and [0041]-[0046] of the Applicants' specification. Support for new claim 15 can be found throughout the specification as filed, for example, in paragraph [0020] of the Applicants' specification. Support for new claim 16 can be found throughout the specification as filed, for example, in paragraphs [0041] of the Applicants' specification. Support for new claim 17 can be found throughout the specification as filed, for example, in paragraphs [0042] of the Applicants' specification. Support for new claim 18 can be found throughout the specification as filed, for example, in paragraphs [0044] of the Applicants' specification. No new matter has been added and entry is respectfully requested.

To further prosecution, Applicant has cancelled without prejudice claims 1-7 and 9-13, rendering the pending rejections moot. Applicant reserves the right to file subsequent applications claiming the canceled subject matter. In addition, the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Response to Objections to the Drawings

In the 2nd paragraph of the Office Action, the Examiner objected to Figures 2, 3 and 6 as being illegible.

In response, Applicants concurrently submit replacement sheets 2 and 3 that include

Figures 2, 3, and 6. In the replacement drawings, Figures 2, 3 and 6 have merely been enlarged to enhance legibility of the drawings. No new material is added in the replacement drawings for Figures 2, 3 and 6 and entry is respectfully requested.

Based on the above amendments and remarks, Applicants respectfully request that the Examiner reconsider and withdraw all objections to the drawings.

Response to Rejection Under 35 U.S.C § 112, second paragraph

In the 3rd paragraph of the Office Action, the Examiner rejects claims 1-7 and 9-13 under 35 U.S.C § 112, second paragraph as indefinite.

Claims 1-7 and 9-12 have been cancelled rendering moot this rejection of the claims. Applicants note that new claims 14-18 do not include the language cited by the Examiner in the indefiniteness rejection, e.g., “comparing” or “using LGA_S analysis” or “apply the transform” or “the calculated alignment.” In addition, Applicants believe the language of the new claims is definite. Withdrawal of this rejection is respectfully requested.

Response to Rejections Under 35 U.S.C § 112, first paragraph (new matter)

In the 4th paragraph of the Office Action, the Examiner rejects claims 1-6 under 35 U.S.C § 112, first paragraph for failing to comply with the written description requirement. The Examiner stated that “Claim 1 introduces new matter as it addresses LGA_S analysis as performed independently of other method steps.”

Without agreeing with the Examiner’s position, Applicant has cancelled claims 1-6 and this rejection is moot. The rejection is not applicable to new claims 14-18. Claims 14-18 do not recite LGA_S analysis performed independently of other method steps. In addition, claims 14-18 are fully supported in the specification as described above.

Accordingly, Applicants request withdrawal of this rejections.

Response to Rejections Under 35 U.S.C § 101 (utility)

In the 5th paragraph of the Office Action, the Examiner rejects claims 1-7 and 9-13 under 35 U.S.C § 101 as allegedly lacking utility. Applicants have cancelled claims 1-7 and 9-13 herein, and traverse the rejection as drawn to the new claims.

In the Office Action, the Examiner reiterated the rejection presented in the Office Action dated January 4, 2007, stating “ ... as a result of computational determination, regions having 3D similarity in two protein molecules are indentified. However, such result lack substantial utility as subsequent research is needed to identify the utility of finding such 3D similarities.”

Applicants respectfully disagree. The claimed invention, a method to generate a score that describes the three-dimensional similarity between 2 protein sequences, has substantial utility. As described in further detail below, the claimed method is not only useful for basic research, e.g., studying the properties of 2 protein sequences. Rather, the method has a real world use that is well-known to one of skill in the art. To support this position, Applicants concurrently submit the Declaration of Carol Ecale Zhou, Ph.D. under 37 C.F.R. § 1.132 (“Zhou Declaration”).

Applicants describe and claim a method for generating local-global alignment score. This score is an example of a protein structure homology score. As is well-known to one of skill in the art, protein structure homology scores are used to characterize similarities between two protein structure in order to identify homologous proteins. Protein structure homology scores are the gold standard in identifying homologous proteins. *See* Zhou Declaration at ¶5.

The protein structure homology score, e.g., the local-global alignment score, generated using Applicants claimed method has a real world, substantial use in public health and drug discovery. *See* Zhou Declaration at ¶7. For example, the local-global alignment score can be used in the field of pathogen detection and identification. Unknown pathogens can be identified

based on the identification of homologous proteins in known pathogens using protein structure homology scores. *See* Zhou Declaration at ¶8. This substantial real-world utility is well-known to one of skill in the art, as evidenced by the Zhou Declaration and by the art cited therein, e.g., the Slezak reference. *See* Zhou Declaration at ¶9.

A further example of the real-world, substantial utility of Applicants invention is in the field of drug discovery. *See* Zhou Declaration at ¶10. The protein structure homology score, e.g., the local-global alignment score, generated using Applicants claimed method can be used to identify proteins in a host organism likely to have cross-reactivity with therapeutics targeted to homologous proteins in a pathogen. Protein structure homology scores are used to identify homologous proteins from a group of pathogens to identify targets for broad spectrum drug development. Again, this substantial, real-world utility is well-known to one of skill in the art, as evidenced by the Zhou Declaration and by the art cited therein, e.g., the Legnauer reference. *See* Zhou Declaration at ¶11.

In conclusion, the claimed method has a substantial, real-world utility, e.g., generating a protein structure homology score for use in public health and drug discovery. This utility is well-known to one of skill in the art. Withdrawal of this rejection is respectfully requested.

Response to Rejections Under 35 U.S.C § 112, first paragraph (enablement)

In the 6th paragraph of the Office Action, the Examiner rejects claims 1-7 and 9-13 under 35 U.S.C § 112, first paragraph; the Examiner stated “Specifically, since the claimed invention is not supported by either a credible asserted utility or a well-established utility, one skilled in the art would not know how to use the claim invention.”

Without agreeing with the Examiner's position, claims 1-7 and 9-13 have been cancelled and this rejection is moot as drawn to those claims. In the interest of advancing prosecution, Applicants address this rejection with regards to newly presented claims 14-18.

Newly presented claims 14-18 are supported by a well-established utility and therefore one of skill in the art would know to use the invention. The pending claims are directed to a method for generating "a local-global alignment score which indicates a global and a local similarity between a first protein structure and a second protein structure," e.g., the pending claims are directed to a method for generating a protein structure homology score. As described above in the Response to the utility rejection, protein structure homology scores have a substantial, real-world utility in public health and drug discovery settings. This utility is well-known to one of skill in the art. Accordingly, the claimed invention is enabled and withdrawal of this rejection is respectfully requested.

Response to Rejections Under 35 U.S.C § 101 (non-statutory invention)

In the 7th paragraph of the Office Action, the Examiner rejects claims 1-7 and 9-13 35 U.S.C § 101 as being directed to non-statutory subject matter.

Without agreeing with the Examiner's position, claims 1-7 and 9-13 have been cancelled. Therefore, these rejections are moot. In the interest of advancing prosecution, Applicants address the rejections with regards to newly presented claims 14-18.

In the Office Action the Examiner stated "As addressed in the rejection, for a claim to be useful the claim must produce a result that is specific, substantial, and credible. As discussed in the utility rejection above, the invention does not satisfy the criteria of utility requirements as not being substantial."

In response, Applicants reiterate the argument made above in response to the utility

rejection. Applicants invention does indeed have a substantial, real-world utility, e.g., generating a protein structure homology score for use in public health and drug discovery. Accordingly, the claimed invention is useful and is directed to statutory subject matter. Withdrawal of the rejection is respectfully requested.

Further, the test for statutory subject matter for a method claim is whether the claim produces a useful, concrete, tangible result. See, *State StreetBank & Trust Co. v. Signature Financial Group*, 149 F.3d 1368; 47 U.S.P.Q.2D (Fed. Cir. 1998), and *AT&T Corp. v. Excel Communications, Inc.*, 172 F.3d 1352, 50 USPQ2d 1447 (Fed. Cir. 1999). In *State Street*, the Court held that the “net asset value” output by computer system was a useful, concrete, tangible result. Similarly, in *AT&T*, the Court held that the determination by computer algorithm of a value for a primary long-distance service (interexchange) carrier was also a useful, concrete, and tangible result.

Claims 14-18 recite useful concrete and tangible results. Newly presented claims 14-18 are directed to a method for generating “a local-global alignment **score** which indicates a global and a local similarity between a first protein structure and a second protein structure.” The generation of this score by way of a computer-algorithm is outlined, for example, in paragraph [0019] of the Specification as a “The system 100 utilizes algorithms and applies the LGA program to test examples in order to highlight some of its features.”

Applicants submit that the local global alignment score provides a concrete, useful and tangible result as it provides a measure of the local and global similarity between two three dimensional protein structures, the protein structures being concrete and tangible real world entities.

Response to Rejection Under 35 U.S.C § 102(b)

In the 8th paragraph of the Office Action, the Examiner rejects claims 1, 2, 4-7 and 10-13 35 U.S.C § 102(b) as allegedly unpatentable over Lackner et. al. (2000) ProSup: a refined tool for protein structure alignment, Protein Engineering, 13911), 745-752 (“Lackner”). Claims 1, 2, 4-7 and 10-13 are cancelled herein. Therefore, the rejection is moot. In the interest of advancing prosecution, Applicants address this rejection as drawn to the newly presented claims.

Newly presented claims 14-18 are directed to a method of generating a local-global alignment score which indicates a global and a local similarity between a first protein structure and a second protein structure. Claim 14 recites in relevant part:

receiving a protein structure correspondence wherein a plurality of positions in the protein structure correspondence indicates a corresponding pair of residues in the first protein structure and the second protein structure;
identifying a longest contiguous segment comprising a plurality of contiguous positions in the correspondence, wherein the root mean square deviation of a set of pairs of residues within the segment is less than a specified threshold value;
identifying a global distance metric based on a number of pairs of residues in the correspondence that are within a pre-determined distance of each other;
generating the local-global alignment score based on the longest contiguous segment and the global distance metric; and
storing the local-global alignment score.

Claims 15-18 depend on claim 14 and include these elements.

In the claimed invention, a protein structure correspondence is received wherein a plurality of positions in the protein structure correspondence indicates a corresponding pair of residues in the first protein structure and the second protein structure (e.g., *see* Specification [0041], “the LGA program generates many different local superpositions to detect regions where proteins are similar”). A longest contiguous segment comprising a plurality of contiguous positions in the correspondence is identified (e.g., *see* Specification [0041] “the LCS procedure is able to localize and superimpose the longest segments of residues that can fit under a selected RMSD cutoff”), wherein the root mean square deviation of a set of pairs of residues within the

segment is less than a specified threshold value (e.g., *see* Specification [0042] “*LCS results are generated for a set of increasing RMSD cutoffs*”). A global distance metric is identified based on a number of pairs of residues in the correspondence that are within a pre-determined distance of each other (e.g., *see* Specification [0042], “*Each calculated superposition is used as a starting point to give an initial list of equivalent residues. The list of equivalent residues is iteratively extended to collect the largest set of residues that can fit under a given distance cutoff.*”). A local-global alignment score based on the longest contiguous segment and the global distance metric is generated and stored (e.g., *see* Specification [0046], “*LCS_{vi} – percent of residues (continuous set) that can fit under an RMSD cutoff of vi A (for vi = 1.0, 2.0 ...), and GDT_{vit} – an estimation of the percent of residues (largest set) that can fit under the distance cutoff of vi A (for vi = 0.5, 1.0, ...). A scoring function (LGA_{vi}) can be defined as a combination of these values and can be used to evaluate the level of structure similarity of selected regions*”).

These elements enable the independent identification of a longest contiguous segment and a global distance metric based on a **same** received correspondence. A score is generated which indicates both local similarity based on the longest contiguous segment and a global similarity based on the global distance metric.

Lackner does not disclose these elements. Lackner discloses a dynamic programming algorithm in which equivalences are iteratively determined and used to generate an optimal superposition. In Lackner, root mean square deviation (RMSD) calculations are used as initial seed parameters which are used to generate an alignment. This alignment is then subject to distance calculations and iteratively refined.

Lackner fails to provide a construction that teaches both “**identifying a longest contiguous segment** comprising a plurality of contiguous positions **in the correspondence**, wherein the root mean square deviation of a set of pairs of residues within the segment is less

than a specified threshold value” and “identifying **a global distance metric** based on a number of pairs of residues **in the correspondence** that are within a pre-determined distance of each other”. In Lackner, root mean square analysis is applied to generate an alignment which is **then** subject to distance analysis. In contrast, in the claimed invention both the longest continuous segment and the global distance metric are identified **independently** based on a **same correspondence**. Therefore, Lackner fails to show both these elements.

Accordingly, the cited reference does not teach each and every element of the claimed invention and cannot anticipate the claimed invention. Withdrawal of this rejection is requested.

CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (415) 875-2316.

Respectfully submitted,
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